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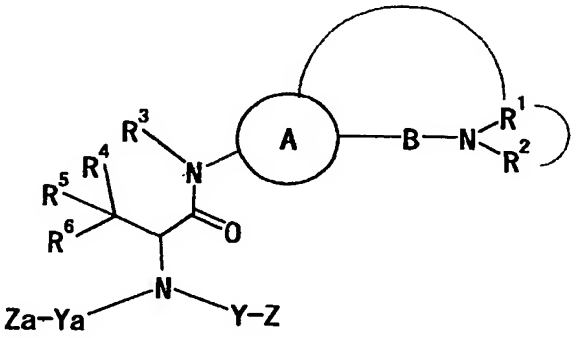
see PCT Gazette No. 31/2004 of 29 July 2004, Section II

[Continued on next page]

(54) Title: IDOLE DERIVATIVES AS SOMATOSTATIN AGONISTS OR ANTAGONISTS



(I)

(57) Abstract: The present invention provide a compound of the formula:wherein ring A represents an aromatic ring optionally having substituents; B, Y and Ya are the same or different and each represents a bond, etc.; R¿1? and R¿2? are the same or different and each represents a hydrogen atom, etc.; R¿3? represents a hydrogen atom, etc.; R¿4? and R¿5? are the same or different and each represents a hydrogen, etc.; R¿6? represents an indolyl group optionally having substituents; and Z and Za are the same or different and each represents a hydrogen atom, etc.; or a salt thereof or a prodrug thereof, having a somatostatin receptor binding inhibition activity and is useful for preventing and/or treating diseases associated with somatostatin.

WO 2004/046107 A1

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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International Application No
PCT/JP 03/14622

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D209/20 C07D401/12 C07D403/12 C07D417/14 C07D495/04
C07D401/14 C07D405/12 C07D417/12 C07D405/14 C07D209/42
A61K31/405 A61K31/454 A61K31/497 A61P3/10 A61P3/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/091090 A1 (HAY BRUCE A ET AL) 11 July 2002 (2002-07-11) paragraph [0013] - paragraph [0056] paragraph [0127] - paragraph [0129] paragraph [0221]; example 21	1-27
X	GB 2 351 733 A (MERCK & CO INC) 10 January 2001 (2001-01-10) claims see definition of t=0 for R3 in claims	1-27
P,X	HERNANDEZ, FERNANDO ET AL: "A short synthesis of de-"prenyl"-ardeemin" TETRAHEDRON LETTERS , 44(16), 3367-3369 CODEN: TELEAY; ISSN: 0040-4039, 2003, XP004417076 compounds 7	1-20

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 June 2004	08. 06. 04

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kollmannsberger, M

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/22577 A (NOVARTIS ERFIND VERWALT GMBH ; NOVARTIS AG (CH); BAIR KENNETH WALTER () 21 March 2002 (2002-03-21) claim 16 page 62; examples 194,197	1-20
X	MALY, DUSTIN J. ET AL: "Expedient Solid-Phase Synthesis of Fluorogenic Protease Substrates Using the 7-Amino-4-carbamoylmethylcoumarin (ACC) Fluorophore" JOURNAL OF ORGANIC CHEMISTRY , 67(3), 910-915 CODEN: JOCEAH; ISSN: 0022-3263, 2002, XP002271450 example 8S; table 1	1-20
X	DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ESCHERICH, ACHIM ET AL: "Peptide/benzodiazepine hybrids as ligands of CCKA and CCKB receptors" XP002271451 retrieved from STN Database accession no. 2001:846593 compound with RN 404391-74-8 & BIOPOLYMERS , VOLUME DATE 2000-2001, 56(2), 55-76 CODEN: BIPMAA; ISSN: 0006-3525, 2001,	1-20
X	WO 01/74844 A (HOFFMANN LA ROCHE) 11 October 2001 (2001-10-11) claim 1 examples 60-62,94-96	1-20
X	WO 01/55106 A (KALVINS IVARS ; KAUSS VALERJANS (LV); STARCHENKOV IGOR (LV); TRAPENCIE) 2 August 2001 (2001-08-02) page 24; example 2.21	1-20
X	DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MERGLER, MONIKA ET AL: "Protected peptide p-nitroanilides by solid-phase synthesis" XP002271452 retrieved from STN Database accession no. 2000:113867 compounds with RN 265327-63-7, 265327-64-8, 265327-70-6, 265327-71-7 & LETTERS IN PEPTIDE SCIENCE , 7(1), 1-7 CODEN: LPSCEM; ISSN: 0929-5666, 2000,	1-20

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BERNHARDT, ANNE ET AL: "The solid-phase synthesis of side-chain-phosphorylated peptide-4-nitroanilides" XP002271453 retrieved from STN Database accession no. 1997:535830 compounds with RN 150933-27-0, 194670-62-7 & JOURNAL OF PEPTIDE RESEARCH , 50(2), 143-152 CODEN: JPERFA; ISSN: 1397-002X, 1997, -----	1-20
X	VARNAVAS A ET AL: "ANTHRANOYL-ANTHRANILIC ACID: A TEMPLATE FOR THE DEVELOPMENT OF A NEW CLASS OF CHOLECYSTOKININ RECEPTOR LIGANDS" PHARMAZIE, VEB VERLAG VOLK UND GESUNDHEIT. BERLIN, DD, vol. 51, no. 10, 1 October 1996 (1996-10-01), pages 697-700, XP002056854 ISSN: 0031-7144 example 1; table 1 -----	1-20
X	MACOR J E ET AL: "The discovery of a novel and potent benzodiazepine receptor pharmacophore" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 5, no. 20, 19 October 1995 (1995-10-19), pages 2397-2402, XP004135272 ISSN: 0960-894X example 1N; table 1 -----	1-20
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; TANAKA, TAKUMI ET AL: "Human leukocyte cathepsin G. Subsite mapping with 4-nitroanilides, chemical modification, and effect of possible cofactors" XP002271455 retrieved from STN Database accession no. 1985:162777 compound with RN 95364-17-3 & BIOCHEMISTRY , 24(8), 2040-7 CODEN: BICHAW; ISSN: 0006-2960, 1985, -----	1-13
X	GB 2 140 423 A (KIMBERLY CLARK CO) 28 November 1984 (1984-11-28) page 10; example 16 -----	1-20
X	DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BABA, YOSHIHIKO ET AL: "N.alpha.-Acyl-.alpha.-L-amino acid anilides" XP002271456 retrieved from STN Database accession no. 1978:191467 compound with RN 66253-15-4 & JP 52 148032 A2 (SANKYO CO., LTD., JAPAN) 8 December 1977 (1977-12-08) -----	1-20
P,X	DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; TAKAHASHI, TOSHIHIRO ET AL: "Preparation of N-phenyl-N-(4-piperidinyl)amide derivatives as peripheral analgesics" XP002271457 retrieved from STN Database accession no. 2003:796661 compounds with RN 608536-05-6, 608536-06-7, 608536-07-8, 608536-08-9 abstract & WO 03/082819 A1 (NIPPON CHEMIPHAR CO.,LTD., JAPAN) 9 October 2003 (2003-10-09) -----	28
X	EP 0 761 220 A (LILLY CO ELI) 12 March 1997 (1997-03-12) page 16 structure IV page 23; example 13 page 24; example 14 -----	28

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 03/14622

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/26188 A (CHRISTNER CLAUDIA ; KUELLERTZ GERHARD (DE); MAX PLANCK GESELLSCHAFT (D) 11 May 2000 (2000-05-11) page 11; example 32	28
X	OJIMA I ET AL: "Design, synthesis and sar of RGD peptide hybrids as highly efficient inhibitors of platelet aggregation" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 5, no. 17, 7 September 1995 (1995-09-07), pages 1941-1946, XP004135341 ISSN: 0960-894X example 5; table 1	28

3

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 03/14622

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 22, 24 and 26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 1-20 (in part); 27 (in part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 22, 24 and 26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 1-20 (in part); 27 (in part)

The claims are so broadly drafted that the initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to:

Compounds and pharmaceuticals of structure (I) in which Z is an optionally substituted cyclic group and A is a phenyl ring, i. e. a combination of claims 5 and 10, thus covering all examples. Use claims 21-26 and claim 28 have been searched completely.

Claim 2 is directed to prodrugs of structurally defined compounds. Since from the term "prodrug" without further definition it is not clear which compounds are actually covered by the claims (Art. 6 PCT) the search with respect to prodrugs has been limited to the possibilities mentioned on pages 50/51 of the description.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/JP 03/14622

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Information on patent family members

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